Spotlight on...

Pascale Cossart

Editor of *FEBS Letters* since 2002

Pascale Cossart has always focussed on following her interests. During her M.Sc., she transferred to Georgetown University (USA) for a year. It was a turning point. "I heard how Frederick Sanger sequenced the protein insulin. I was fascinated, quite frankly," she says, "for me it was the beauty of chemistry applied to biology." Her PhD (Pasteur Institute, Paris) followed, during which she sequenced an *E. coli* protein. Through the following years, her research interests continued evolving, from sequencing proteins to sequencing genes, to studying DNA–protein interactions, and finally, tackling the problem of pathogenicity. Pascale is currently the Director of the Cell Biology and Infection Department, and Head of the Bacteria-Cell Interactions Unit at the Pasteur Institute (Paris, France). She is also the foremost authority on food-borne pathogen *Listeria monocytogenes*. Pascale edits for *FEBS Letters* papers dealing with microbiology, toxins, bacterial invasiveness, and actin-based motility.

What does your lab do?

We decipher the molecular mechanisms that underlie virulence, using the bacterial pathogen *Listeria monocytogenes* as a model organism, and one of our goals is to generalize our discoveries to other pathogenic bacteria. We identify and characterize components that are critical for infection, in both the bacteria and the host, and investigate their interactions, and the resulting signals. We want to understand the time-scale of the signalling events. We validate our results in animal models, with knock-out and transgenic mice. Our lab is multidisciplinary. We use techniques from molecular biology, biochemistry, cell biology, post-genomics and also transgenesis.

How does a pathogenic bacterium invade cells?

If a *Listeria* bacterium reaches the intestinal tract, it can induce intestinal cells to phagocytose it in a vacuole. The bacterium then lyses the vacuole and moves actively throughout the cell, dividing and multiplying. Sometimes, one or more of these bacteria will push a protrusion into a neighbouring cell and invade it too. So tissues are infected, by direct cell to cell. The bacteria are clever enough to induce anti-apoptotic mechanisms during this process. Pathogenic bacteria do not want to be too virulent, they need somewhat healthy cells!

Virulence and pathogenicity, what is the difference?

An organism is pathogenic when it is capable of harming its host, while virulence refers to the degree of harm caused. The level of this interaction depends both on the organism and the host. For instance, a bacterium can be virulent for you but not for me, because I might have a better innate immune response.

Will a pill ever be developed protect vacationers and travellers from bacterial infections?

I would not advise taking such an anti-bacterial pill, because commensal bacteria are in your body, that are critical for your innate immune response. It is important to keep the antibacterial drugs for when a real robust infection occurs. The emerging problem is that more and more bacteria are resistant to antibiotics. And this is why it is important for researchers like us to pave the way for new drugs.

What discoveries could lead to new drugs?

Understanding, for instance, how a bacterium enters a cell and circumvents the innate immune response. Our research has already resulted in an unexpected discovery; one that may help in treating cancer. We just deposited a patent dealing with the interaction between the bacterial protein InlB and the growth factor receptor, Met [1]. We noticed that InlB causes Met to endocytose much more quickly than a normal ligand does. We also knew that in many types of cancer, this receptor has a mutation that constitutively activates it, so the ability to downregulate this receptor may have an application as an anti-cancer drug.

What do you consider your best papers?

Our 1992 Cell paper was ground-breaking because it describes ActA, a protein that mediates actin-based motility in Listeria [2]. This discovery was a happy accident, we found this gene when we were looking for lecithinase mutants, and stumbled across one that was totally avirulent, and completely non-motile inside mammalian cells. The actA gene and the lecithinase gene are part of the same operon, hence the phenotype of our mutant! Our 1996 Cell paper reports E-cadherin as the receptor that Listeria binds to before entering cells [3]. It was perfect hindsight to find that Listeria indeed uses this molecule. I had previously heard Rolf Kemler give a talk about E-cadherin at a conference, and I thought that it would make the ideal receptor for a pathogen. And it is amazing that E-cadherin was discovered here at the Pasteur Institute [4]. Prime examples of serendipity.

References

[1] Veiga, E. and Cossart, P. Patent number: DI 2004-112 (France), 03495-6107. US provisional patent application.
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0014-5793/$32.00
doi:10.1016/j.febslet.2007.01.001